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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,182	09/21/2005	Mats Inganas	HO-P02774US1	8048
26271	7590	06/18/2010		
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EXAMINER				
HURST, JONATHAN M				
ART UNIT		PAPER NUMBER		
1797				
NOTIFICATION DATE		DELIVERY MODE		
06/18/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/550,182

Applicant(s)

INGANAS, MATS

Examiner

JONATHAN M. HURST

Art Unit

1797

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 9-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 9-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-06)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-7, 9-12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mian et al. (US 6,319,469) in view of Sucholeiki (US 5,858,534).

Regarding claims 1, 4, and 15 Mian et al. discloses a collection of one or more microfluidic devices which together carry a plurality of microchannel structures each of which comprises a reaction microcavity in which there is a solid phase, a porous bed of paramagnetic bead particles, with an immobilized affinity ligand L, (See Fig. 1A, Fig. 1C, Fig. 17L, and Col. 43 Lines 25-40), wherein

(i) the plurality comprises two or more different sets of microchannel structures, (See Fig. 17L where each disk layer comprises a set of different channels Fig. 17A where disk contains sets of different channels and Col. 33 Lines 33-36 where a device performs a set of procedures or multiple embodiments of the same procedure), and

(ii) the affinity ligand L is directed to the same counterpart (binder, B) independent of set, and (See Col. 33 Lines 33-36 where sets of the same procedure are performed) and

(iii) the sets differ with respect to

a) the capacity for binder B per reaction microcavity and/or the capacity per unit volume of the solid phase in a reaction microcavity, and/or (See Col. 8 Lines 30-35 where reservoirs act as microcavity and sizes differ depending upon embodiment and thus have different capacities for reagents) and

b) the base matrix of the solid phase between the sets but are equal within each set. (See Fig. 17L where base is different for each set of channels)

The microchannels, and reaction microcavity, have surfaces exposing a plurality of polar functional groups such that the surfaces of the walls are hydrophilic (See Col. 14 Line 45 – Col. 15 Line 45 where the walls of the microchannels and of microcavities are modified to have hydrophilic surfaces with polar functional groups to improve adsorption of specific materials) especially since the materials used are modified to have hydrophilic groups and thus the microchannels and microcavities, which are etched from the walls, would also have hydrophilic surfaces.

Mian et al. also discloses the collection wherein said reaction microcavity in at least one of said microchannel structures in the upstream direction is connected to a volume- metering unit. (See Fig. 13B and Col. 26 Lines 15-24 also See Fig. 1A where an inlet channel 11 and/or 16 can be used to meter a volume of fluid if one so wished and is thus a volume metering unit).

Main does not specifically disclose the solid phase being a porous bed of particles having surfaces exposing a plurality of polar functional groups such that the surfaces of the particles are hydrophilic.

Sucholeiki discloses paramagnetic beads, used for binding ligands in chemical sensing applications, which have surfaces exposing a plurality of polar functional groups such that said surfaces are hydrophilic. (See Abstract and Col. 3 Lines 28-56)

It would have been obvious to one of ordinary skill in the art at the time of invention to use paramagnetic beads with hydrophilic surfaces as described by Sucholeiki in the device of Mian et al. because such paramagnetic beads are known in the art to be used in chemical sensing applications as is required by Mian in order to provide more preferable conditions for linking a ligand to said paramagnetic beads.

Regarding claim 2, modified Mian discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the collection wherein at least one

of the sets of the collection have a binding capacity difference with a factor ≥ 1.2 compared to the binding capacity for the set having the lowest binding capacity. Altering the binding capacities in different sets of microchannels/microcavities allows for more specific reaction and analysis of a wide range of sample types and concentrations and the precise binding capacity differences would have been considered a result effective variable by one having ordinary skill in the art at the time the invention was made. As such, without showing unexpected results, the claimed binding capacity difference factor cannot be considered critical. Accordingly, one of ordinary skill in the art at the time the invention was made would have optimized, by routine experimentation, the binding capacity difference factor in the apparatus of Mian et al. to obtain the desired analytic and reactive capabilities of the device. (In re Boesch, 617 F.2d. 272, 205 USPQ 215 (CCPA 1980)), since it has been held that where the general conditions of the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (In re Aller, 105 USPQ 223).

Regarding claim 3 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein at least one of said devices comprises

- a) at least two of said sets of microchannel structures, and/or
- b) only one set of microchannel structures, with the proviso that the collection comprises two or more devices which are different with respect to the kind of sets

they carry. (See Fig. 17L where device contains more than one layer and set of microchannel structures).

Further regarding limitations recited in claim 4 which are directed to a manner of operating disclosed collection, it is noted that neither the manner of operating a disclosed device nor material or article worked upon further limit an apparatus claim. Said limitations do not differentiate apparatus claims from prior art. See MPEP § 2114 and 2115. Further, it has been held that process limitations do not have patentable weight in an apparatus claim. See *Ex parte Thibault*, 164 USPQ 666, 667 (Bd. App. 1969) that states "Expressions relating the apparatus to contents thereof and to an intended operation are of no significance in determining patentability of the apparatus claim."

Regarding claim 5 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein L is selected amongst biotin-binding compounds and streptavidin-binding compounds, respectively, or vice versa. (See Col 43 Lines 30-37 biotin binding streptavidin is used).

Regarding claim 6 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein L has two or more binding sites for B. (See Col 43 Lines 30-37 biotin binding streptavidin is used and it is inherent that streptavidin has more than one binding site for biotin).

Regarding claim 7 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein

- (a) that each set on a device is grouped into one or more groups of fluidly equivalent microchannel structures, and (See Fig. 17L where sets on each layer are groups of fluidly equivalent microchannel structures) and
- (b) that each group is located to a particular subarea of the device. (See Fig. 17L where each layer is a subarea of the device and contains a group)

Regarding claim 9 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein said volume-metering unit is part of an inlet arrangement for liquid. (See Fig. 13B and Col. 26 Lines 15-24)

Regarding claim 10 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein said reaction microcavity in at least one of said microchannel structures in the upstream direction is connected to a volume-metering unit and wherein said volume-metering unit within at least one of said group(s) is part of a distribution manifold for distributing liquid to the reaction microcavities of the group, with the proviso that each of said at least one group comprises two or more microchannel structures. (See Fig. 13B and Col. 26 Lines 15-24 where multiple samples are dispensed to a group of microchannels using volume-metering units).

Regarding claim 11 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein the inner wall of each of said volume-metering units has a sufficient hydrophilicity for said unit to filled by capillarity once an aqueous liquid have entered the unit, and b) a valve at its outlet end,. (See Col. 26 Lines 15-24 where volume metering units have appropriate specific surface properties and Col. 14 Lines 45-55 where hydrophilicity is a surface property and Col. 17 Lines 38-41 where fluid movement is controlled by valves).

Regarding claim 12 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein at least one of the solute S and its affinity counterpart ACs, and/or at least one of the binder B and the ligand L comprise a structure selected from the group_of amongst peptide structure consisting of including poly/oligo-peptide and protein structure, carbohydrate structure, lipid structure including steroid structure, nucleotide structure including nucleic acid structure, and polymeric structure. (See Col. 43 Lines 30-34).

Further regarding limitations recited in claim 12 which are directed to a manner of operating disclosed collection, it is noted that neither the manner of operating a disclosed device nor material or article worked upon further limit an apparatus claim. Said limitations do not differentiate apparatus claims from prior art. See MPEP § 2114 and 2115. Further, it has been held that process limitations do not have patentable weight in an apparatus claim. See Ex parte Thibault, 164 USPQ 666, 667 (Bd. App. 1969) that states "Expressions relating the apparatus to contents thereof and to an

intended operation are of no significance in determining patentability of the apparatus claim.”

4. Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mian et al. (US 6,319,469) in view of Sucholeiki (US 5,858,534) as applied to claims 1-12 and 15 above in view of Jacobs et al. (US 2002/0095073)

Regarding claims 13 and 14 modified Mian et al. discloses all the claim limitations as set forth above as well as the collection wherein said solid phase is in a dry state (See Col. 39 Line 65- Col. 40 Line 2 where disk is dried) but does not disclose the collection comprising in addition to the solid phase one or more bed preserving agents or wherein at least one of said one or more bed-preserving agents is a microcavity adherence agent.

Jacobs et al. describes the use of a bed preserving agents wherein bed-preserving agents is a microcavity adherence agent. (See [0019] where cross-linked straptavidin is immobilized as a preserving agent)

It would have been obvious to one of ordinary skill in the art at the time of invention to use the bed preserving agent of Jacobs in the collection of Main because doing so helps preserve and stabilize the biological activity of the device. (See Jacobs [0019]).

Response to Arguments

5. Applicant's arguments filed 03/25/2010 have been fully considered but they are not persuasive.

Applicant argues on pages 5-6 of the response that "The present invention according to amended claim 1 (which now incorporates the subject matter of claim 8) differs from Mian at least in that the "reaction microcavity in at least one of said microchannel structures in the upstream direction is connected to a volume- metering unit located to a particular subarea of the one or more microfluidic devices"" and "Mian discloses the use of positive or negative pressure to move liquid aliquots from the volume-metering unit to the microchannel structures (col. 26, lines 15-28). This transfer of liquid is by definition done after volume-metering, and accordingly there is a risk for contamination, sample losses due to evaporation, etc. This teaches away from the present invention, which enables volume-metering and subsequent liquid handling steps to be handled in a single device. In particular, the volume defining step is done on the device, not in an external autosampler as with Mian. This is a significant technological difference, because it would not be practical to apply the volume defining unit of Mian directly on the microfluidic device."

It is the examiner's position that Mian et al. does in fact disclose a volume-metering unit. See Fig. 13B and Col. 26 Lines 15-24 where a volume metering unit such as a pipette and/or syringe is connected to a microcavity in an upstream direction and is used to meter a volume of fluid into said device. Also see Fig. 1A where an inlet

channel 11 and/or 16 integrally formed within the device is connected to a microcavity in an upstream direction and can be used to meter a volume of fluid if one so wished and is thus a volume metering unit.

It is noted that applicant appears to be arguing that the claimed volume-metering unit is formed integrally, i.e. such as by molding, with the microchannel but the claim does not require such a limitation. The claim as presently presented merely requires that the volume-metering unit be connected to a microchannel structure in an upstream direction.

Furthermore it is noted that applicant does not describe claim any specific structure relating to the elements which make up a volume metering unit and as such a volume-metering unit is broadly interpreted to be any structure which is capable of holding a fluidic volume and transferring said volume to a microcavity through some form of connection.

Applicant argues on page 6 of the response that "Mian also teaches away from Sucholeiki, and, therefore, the skilled artisan would have no reason to combine the elements therein to achieve the claimed invention. The claimed invention utilizes particles having surfaces exposing a plurality of polar functional groups such that the surfaces are hydrophilic. Mian teaches away from both Sucholeiki and the claimed invention by teaching the skilled artisan to employ a solid phase with Dynabeads, which are hydrophobic. No skilled artisan would combine Sucholeiki and Mian, particularly because such beads would drastically alter the properties of Mian, and if a proposed

modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Furthermore, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, as it would be utilizing beads of wholly opposite chemistry, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)."

It is the examiner's position that the combination of references as disclosed in the rejections above is proper. It is noted that while the one type of specific paramagnetic beads disclosed by Mian may be hydrophobic said beads appear to be merely provided as a non-limiting example of such beads. Mian does not suggest nor clearly discourage the use of other types of beads, i.e. such as those described by Sucholeiki, and as such Mian does not teach away from the beads of Sucholeiki. Sucholeiki discloses that it is advantageous to provide hydrophilic beads in place of the known hydrophobic beads, such as those given in a non-limiting example by Mian, in ligand binding assays. Since Sucholeiki discloses the use of such beads in ligand binding assays, such as those described by Mian, it is the examiner's position that one of ordinary skill in the art at the time of invention would have been motivated to use beads described by Sucholeiki in the device of Mian.

Furthermore it is noted that applicant provides no evidence that the beads disclosed by Sucholeiki would render the prior art invention being modified unsatisfactory for its intended purpose. Burden is upon applicant to show that the beads described by Sucholeiki could not be used in a ligand binding assay such as those described as being performed in the device of Mian.

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007).

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JONATHAN M. HURST whose telephone number is (571)270-7065. The examiner can normally be reached on Mon. - Thurs. 6:30-4:00; Every other Fri. off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571)272-1374. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. M. H./

Examiner, Art Unit 1797

/Angela Ortiz/

Supervisory Patent Examiner, Art Unit 1797